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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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DARBY & DARBY
805 THIRD AVENUE
NEW YORK, NY 10022

EXAMINER

BARTON, JEFFREY THOMAS

ART UNIT	PAPER NUMBER
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1753

DATE MAILED: 08/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/928,590

Applicant(s)

SPENCE ET AL.

Examiner

Jeffrey T. Barton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-18, 21-36 and 39-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-18, 21-36 and 39-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 7 April 2005 was filed after the mailing date of the Non-Final Action on 3 November 2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, copies of non-patent literature references numbered 0066-0076 and 0078-0099 were not found in the file of the parent case 09/325,667. Applicant is kindly requested to provide copies of these references for consideration.

Response to Amendment

2. The amendment filed on 18 May 2005 does not place the application in condition for allowance.

Status of Objections and Rejections Pending Since the Office Action of 3 November 2004

3. All objections and rejections of claims 19, 20, 37, and 50 are obviated due to cancellation of the claims.

4. The objection to claim 43 is withdrawn

5. The rejection of claims 51, 52, 7, 8, 14, 15, and 28-30 under 35 U.S.C. §102(e) as anticipated by Ramsey et al is maintained.

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6. The rejection of claim 9 under 35 U.S.C. §102(a) as anticipated by Blankenstein is maintained.
7. The rejection of claim 3 under 35 U.S.C. §103(a) as unpatentable over Ramsey in view of Parce et al (US 5,779,868) is maintained.
8. The rejection of claims 4, 6, and 53 under 35 U.S.C. §103(a) as unpatentable over Ramsey in view of Parce et al (US 5,885,470) is maintained.
9. The rejection of claims 22-24, 35, and 36 under 35 U.S.C. §103(a) as unpatentable over Ramsey in view of Asgari et al is maintained.
10. The rejection of claims 54, 43-46, and 49 under 35 U.S.C. §103(a) as unpatentable over Ramsey is maintained.
11. All other previous rejections are withdrawn due to Applicant's amendment.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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13. Claims 51, 52, 7, 8, 14, 15, and 28-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Ramsey et al.

Regarding claim 51, Ramsey et al disclose a device (Figures 16 and 17) comprising a substrate having an analysis unit microfabricated thereon (Column 3, lines 23-27), comprising: a main channel with an inlet, detection region downstream of the inlet (Column 7, lines 43-46), and a branch point discrimination region adjacent to and downstream of the detection region (Figures 16 and 17); two branch channels originating at the branch point in communication with the main channel (Figures 16 and 17); and a flow control system responsive to the detection apparatus (Column 7, lines 43-46), adapted to direct biological material into a selected branch channel (Column 7, lines 25-60), with the capability to reverse the flow direction. (Column 5, lines 2-5)

Regarding claim 52, Ramsey et al disclose a device where the flow control is responsive to a detector responsive to a characteristic of the analyte. (Column 7, lines 43-46, 56-60)

Regarding claims 7 and 8, Ramsey et al disclose electrophoretic and electroosmotic flow control. (Column 6, lines 36-50)

Regarding claims 14 and 15, Ramsey et al disclose flow control by a voltage gradient between the branch channels and junction, caused by electrodes in the branch channels. (Column 3, lines 62-64; Column 8, lines 50-53)

Regarding claim 20, Ramsey et al disclose reversible flow. (Column 5, lines 2-5)

Regarding claims 28-30, Ramsey et al disclose a detection apparatus comprising source and detector (CCD) for electromagnetic radiation. (Column 3, line 65 - Column 4, line 4)

14. Claims 51, 52, 54, 2, 3, 5, 8-10, 13, 16-18, 21, 22, 25-29, 31-36, 39-43, and 47-49 are rejected under 35 U.S.C. 102(a) as being anticipated by Blankenstein.

Regarding claim 51, Blankenstein discloses a device (Figure 8) comprising a substrate having an analysis unit microfabricated thereon (Page 19, lines 24-31), comprising: a main channel (5) with an inlet, detection region downstream of the inlet (adjacent to microscope objective 16), and a branch point discrimination region (where channels 6 and 7 split) adjacent to and downstream of the detection region; two branch channels originating at the branch point in communication with the main channel (6 and 7); and a flow control system responsive to the detection apparatus (Page 24, lines 29-34), adapted to direct biological material into a selected branch channel (Page 24, lines 29-36), with the capability of reversing the flow direction. (Page 24, line 36 - Page 25, line 4)

Regarding claim 52, Blankenstein discloses a flow control system responsive to a detection apparatus for evaluating the material according to a characteristic. (Page 24, lines 29-34)

Regarding claim 54, Blankenstein discloses a method of using his device, the method comprising: flowing a sample of cells through the main channel so that one cell at a time passes the detection region (Page 24, lines 24-26; Page 3, lines 30-31);

interrogating each cell for a characteristic as it passes (Page 24, lines 29-30); and directing the flow of each cell into a branch channel according to the results of the interrogation. (Page 24, lines 31-36)

Regarding claim 2, Blankenstein discloses a reservoir communicating with a branch channel. (Figure 8, chamber 37)

Regarding claim 3, Blankenstein discloses using a silicon substrate. (Page 19, lines 19-26)

Regarding claim 5, Blankenstein discloses the biological material comprising cells. (Page 18, lines 22-25)

Regarding claims 8, 9, and 43, Blankenstein discloses electrophoretic and dielectrophoretic flow control. (Page 9, lines 15-20)

Regarding claims 10 and 43, Blankenstein discloses pressure-driven flow. (Figure 8, syringes cause flow)

Regarding claims 13 and 43, Blankenstein discloses flow-stoppage-based control. (Page 24, lines 31-36)

Regarding claims 16, 43, and 47, a pressure gradient inherently causes flow in the flow control method described at Page 24, lines 31-36.

Regarding claims 17 and 48, capillary action will inherently be present when flowing fluid between passages with differing cross section, as in the device shown in Figure 8. (e.g. Junction of channel 6 with chamber 37)

Regarding claims 18 and 49, Blankenstein discloses using valves for flow control. (Figure 8, valves 43 and 44)

Regarding claims 21, 22, 25, 40, and 42, Blankenstein discloses optical detection of fluorescently labeled analytes. Such fluorescent labels are spectroscopically detectable. (Page 24, lines 8-18)

Regarding claim 26, Blankenstein discloses separation of cells according to size. (Page 19, lines 33-35)

Regarding claim 27, any surface on which the light impinges will cause scattering to some extent.

Regarding claims 28, 29, and 41, Blankenstein discloses using a light source and photomultiplier tube detector. (Page 24, lines 8-18)

Regarding claim 32, Blankenstein discloses such positioning of the detector. (Figure 8, objective 16 with associated PMT)

Regarding claims 33, 34, and 39, Blankenstein discloses channel widths of 100-550 microns, with depths of 40-200 microns. (Page 20, line 33) Dimensions in the hundreds of microns correspond to the claimed dimensions, for separation of most mammalian cells.

Regarding claims 35 and 36, Blankenstein discloses separation due to fluorescent agents associated with the cells (Page 24, lines 8-9; Figure 7)

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al in view of Parce et al. (U.S. 5,779,868)

Ramsey et al disclose a device as described above in addressing claim 51.

Ramsey et al do not explicitly disclose constructing the channels in a silicon substrate.

Parce et al disclose fabrication of capillary channels for analytical devices in a silicon substrate using well-known lithographic techniques. (Column 4, lines 6-56)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Ramsey et al by fabricating the substrate from silicon, as taught by Parce et al, because the lithographic techniques were well-known, reliable, and suitable for large-scale production.

19. Claims 4, 6, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al in view of Parce et al. (US 5,885,470)

Ramsey et al disclose a device as described above in addressing claim 51.

Ramsey et al do not explicitly disclose constructing the channels from silicone elastomers (Claim 4) or specifically polydimethylsiloxane (PDMS) (Claim 53); or molding the substrates by impression from an etched silicon mold. (Claim 6)

Parce et al disclose molding substrates with capillary channels for analytical devices from silicone elastomers (specifically PDMS) (Column 5, lines 16-67), and molding the devices by impression from an etched silicon wafer mold. (Column 13, lines 44-57)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Ramsey et al by replacing his glass

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substrate for a PDMS substrate molded against an etched silicon mold, as taught by Parce et al, because it would allow low-cost, large scale fabrication of the devices.

20. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blankenstein.

Blankenstein discloses a device as described above in addressing claim 51. Blankenstein also discloses using valves in controlling fluid flow. (Figure 8, valves 43 and 44)

Blankenstein does not explicitly disclose using a "microvalve" for flow control.

However, particularly as there is no disclosure in the instant specification concerning any properties or requirements of such a "microvalve", this limitation is taken to be simply directed to the size of features of such a valve. One having ordinary skill in the art would certainly be motivated to use valves with channel dimensions on the order of the capillary dimensions (i.e. tens or hundreds of micrometers, like channels 5-7), in order to obtain precise flow control. Such valves could accurately be called "microvalves" based on this dimension. Furthermore, in *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

21. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blankenstein in view of Gourley et al.

Blankenstein discloses a device as described above in addressing claim 51. Blankenstein also discloses using various forces to sort cells, including magnetic, gravitational, and hydrodynamic forces.

Blankenstein does not explicitly disclose separation of cells using optical trapping.

Gourley et al disclose a similar cell sorting device wherein cells of different types are directed towards their desired destination using optical trapping. (Column 7, line 50 - Column 8, line 7)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Blankenstein by incorporating a device to aid in sorting cells using optical trapping, as taught by Gourley et al, because Gourley teaches the effectiveness of using optical trapping for cell sorting, and one having ordinary skill in the art would have recognized that superior precision would be attainable with optical trapping, as direct manipulation of a cell is used in sorting, as opposed to control of the flow of a fluid in which the cell is suspended.

22. Claims 22-24, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al in view of Asgari et al.

Ramsey et al disclose a device as described above in addressing claim 51.

Relevant to claims 22 and 35, Ramsey et al also disclose detection of fluorescence from analytes. (Column 4, lines 1-9)

Relevant to claim 36, Ramsey et al disclose electroosmotic and electrophoretic flow control. (Column 6, lines 35-50)

Ramsey et al do not explicitly disclose detection and selection of cells based on fluorescent, chemiluminescent, or radioactive reporters (Claims 22-24), nor do they disclose labeling cells for analysis with a fluorescent label (or any label). (Claim 35)

Asgari et al disclose labeling, detection, and selection of cells labeled with fluorescent, chemiluminescent or radioactive reporters. (Column 3, lines 18-21; Column 21, line 54 - Column 22, line 35)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Ramsey et al by labeling cells to be analyzed with characteristic reporters (and providing suitable detectors), as taught by Asgari et al, because such detection methods are conventional, and it would allow the device to be used to analyze a wider variety of cells, and separate them based on a wider variety of characteristics. In addition, fluorescent labels would provide especially convenient interrogation means, given the disclosed detector of Ramsey et al.

23. Claims 54, 43-46, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey et al.

Relevant to claim 54, Ramsey et al disclose a method of using their device (See paragraph 6 above), the method comprising: flowing a sample of cells through the main

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channel (Figures 16 and 17; Column 7, lines 42-46); interrogating each cell for a characteristic as it passes (Column 7, lines 43-46); and directing the flow of each cell into a branch channel according to the results of the interrogation. (Column 7, lines 43-46)

Relevant to claim 43, Ramsey et al disclose flow control by electroosmosis and electrophoresis. (Column 6, lines 35-50)

Relevant to claims 44-46, Ramsey et al disclose flow control by voltage gradients between the branch channels and the junction, caused by electrodes in the branch channels and the main channel. (Column 3, lines 62-64; Column 8, lines 50-53)

Relevant to claim 49, Ramsey et al disclose reversible flow. (Column 5, lines 2-5)

Ramsey et al do not explicitly disclose a method wherein the cells pass the detector one at a time, on average.

It would have been obvious to one having ordinary skill in the art to modify the method of Ramsey et al by providing the degree of focusing and channel dimensions such that the sample stream allows only one cell at a time to pass the detector, because it would maximize the accuracy of the cell sorting method. Given the dimensions of the channels described (Column 3, lines 49-55), and the narrowness of the focused stream (Column 5, lines 32-40; Column 6, lines 40-47), this would be within the skill of one of ordinary skill.

Response to Arguments

24. Applicant's arguments filed 18 May 2005 have been fully considered but they are not persuasive.

With summaries contrasting the respective disclosures with the instant specification, Applicant argues that neither Ramsey et al nor Blankenstein disclose a device that meets the added limitations to a flow control system "responsive to a detection apparatus and adapted to reverse the direction of movement of a biological material."

The Examiner acknowledges that differences exist between the disclosures of the prior art documents and the instant application. However, in order for these to be the basis of patentability, they must be reflected in the language of the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regarding Applicant's assertion that neither Ramsey et al nor Blankenstein disclose a flow control system responsive to a detection apparatus, the Examiner disagrees. Both Blankenstein (Page 24, lines 31-36) and Ramsey et al (Column 7, lines 43-46) clearly disclose flow control responsive to a detector.

Regarding the limitation that the device be "adapted . . . to reverse the direction of movement of biological material that has been directed into a selected branch channel", the Examiner considers this limitation to be directed to an intended use of the device. A recitation of the intended use of the claimed invention must result in a

structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). In the present case, both Blankenstein (Page 24, line 36 - Page 25, line 4) and Ramsey et al (Column 5, lines 2-5) disclose reversed flow within their devices, which indicates that these devices would be capable of performing the intended use.

Conclusion

25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

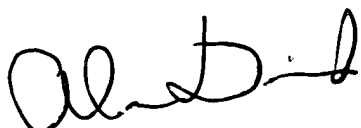
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26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
August 2, 2005


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